Real-world effectiveness of topical ruxolitinib in non-segmental vitiligo: repigmentation, mental health, and quality-of-life outcomes in an 860-patient multicentre study

Running head: Ruxolitinib in vitiligo: real-world outcomes

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Data availability: Due to restrictions on the data used in this study for reasons of patient consent, requests for data access should be addressed to silvia.alberti@unimi.it.

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Patient consent: Written patient consent for publication was obtained.

What's already known about this topic?

- Topical ruxolitinib 1·5% demonstrated effectiveness in the TRuE-V1 and TRuE-V2 phase 3 trials, achieving F-VASI75 in 30% of patients at 24 weeks in selected populations.
- Real-world effectiveness in older, pre-treated patients with higher comorbidity burden remains poorly characterised.

- Clinical predictors of treatment response in unselected populations have not been systematically evaluated.

What does this study add?

- In 860 real-world patients, F-VASI75 was 18·5% at 24 weeks, with progressive repigmentation through 52 weeks;anxiety, depression, and disease-specific quality of life improved in parallel.
- In multivariable analysis, summer treatment initiation and Koebner phenomenon were independently associated with 24-week response; these exploratory findings may help identify patients likely to benefit from early treatment. Adverse events were mild in 98·9% of cases; discontinuation rate was 1·5%.

Abstract

Background: Vitiligo affects 0·5–2% of the global population and carries a substantial psychosocial burden. Topical ruxolitinib 1·5% cream is approved for non-segmental vitiligo based on phase-3 trial data, but real-world evidence across heterogeneous populations remains limited.

Objectives: To evaluate the real-world effectiveness, safety, and patient-reported outcomes of topical ruxolitinib across 34 Italian dermatology centres, and to identify possible clinical predictors of treatment response.

Methods: Multicentre retrospective cohort study (July 2024–October 2025). Patients (≥12 years) with non-segmental vitiligo received ruxolitinib 1·5% cream twice daily. Primary outcomes were F-VASI75 and F-VASI90 at 24 and 52 weeks. Secondary outcomes were VNS, DLQI, VitiQoL, GAD-7, and PHQ-9.

Results: 860 patients (mean age 47 years; 58% female; disease duration 13·5 years; 84% previously treated) completed 24-week assessment; 229 (26·6%) had reached 52 weeks at the time of data lock. F-VASI75 was achieved by 18·5% at 24 weeks, increasing to 38·4% at 52 weeks; F-VASI90 rose from 5·7% to 25·8%. In multivariable logistic regression, summer treatment initiation (adjusted OR 6·7, 95% CI 2·7–16·8) and Koebner phenomenon (adjusted OR 1·6, 95% CI 1·04–2·66) were independent predictors of F-VASI75 at 24 weeks. At baseline, 37% of patients had moderate-to-severe anxiety (GAD-7 ≥10); this fell to 11% at 24 weeks and 2% at 52 weeks. VitiQoL, DLQI, and PHQ-9 improved at all timepoints. Adverse events were mild in 98·9%; treatment discontinuation rate was 1·5%.

Conclusions: In a large real-world population considerably more heterogeneous than registration trial cohorts, topical ruxolitinib showed progressive repigmentation through 52 weeks with excellent tolerability. Summer initiation and Koebner phenomenon independently predicted early response, findings that may inform patient counselling and the design of prospective studies. The parallel sustained reduction in anxiety and depression argues for standardised mental health assessment as a routine component of vitiligo care.

Introduction

Vitiligo affects 0·5–2% of the population globally, characterised by progressive melanocyte loss with profound psychosocial impact.[1–3] Until recently, treatment options were limited to topical corticosteroids, calcineurin inhibitors, and phototherapy, with variable efficacy.[4]

The identification of the interferon-gamma (IFN-γ)/CXCL10 axis and JAK-STAT signalling as central to vitiligo pathogenesis[5–7] led to development of topical JAK inhibitors. Ruxolitinib 1·5% cream, approved by the FDA in 2022[8] and available in Italy since May 2024 following EMA approval,[9] demonstrated efficacy in the TRuE-V1/2 trials.[10]

Whether trial efficacy translates to routine clinical practice remains uncertain. Available real-world evidence consists of small single-centre studies with follow-up of 12–24 weeks,[11-14] and a social media infodemiology analysis,[15] none of which addresses psychosocial outcomes. The TRuE-V trials evaluated Dermatology Life Quality Index (DLQI) and Vitiligo Noticeability Scale (VNS) but not standardised mental health or vitiligo-specific instruments, and how psychological well-being evolves alongside clinical repigmentation during JAK inhibitor therapy remains unknown.

We conducted a large multicentre retrospective study to evaluate real-world effectiveness and safety of topical ruxolitinib in Italian clinical practice, identify clinical associations with treatment response, and assess the impact of treatment on standardised mental health and quality-of-life outcomes.

Patients and methods

Study design and patient selection

This multicentre retrospective cohort study enrolled patients from 34 Italian dermatology centres between July 2024 and October 2025. Institutional review board approval was obtained and written informed consent was provided by all patients.

Eligible patients were aged ≥12 years with clinical diagnosis of non-segmental vitiligo receiving topical ruxolitinib 1·5% cream twice daily. Of 1,129 patients enrolled, 860 (76·2%) had completed 24-week assessment and were included in the primary analysis; 229 (26·6%) had reached 52 weeks at the time of data lock, reflecting the progressive enrolment timeline rather than treatment discontinuation or loss to follow-up. A further 269 patients were excluded as only baseline data were available (Patient flow in Figure S1).

Baseline variables collected included demographics, Fitzpatrick phototype, ethnicity, disease characteristics, medical history, and previous vitiligo treatments. Disease activity was defined as Vitiligo Signs of Activity Score (VSAS)>0 or the presence of new or enlarging lesions within the preceding 6 months, based on standardised photography.[16]

Outcomes and assessments

At baseline, weeks 24, and 52, we recorded facial Vitiligo Area Scoring Index (F-VASI), total-body VASI (T-VASI), VNS, VSAS, DLQI, and Vitiligo-specific Quality of Life (VitiQoL). Primary outcomes were percentage of patients achieving ≥75% (F-VASI75) and ≥90% (F-VASI90) improvement from baseline in F-VASI at 24 and 52 weeks.

Mental health was assessed using the Generalised Anxiety Disorder 7-item scale (GAD-7)[17] and the Patient Health Questionnaire-9 (PHQ-9),[18] with a reduction of ≥4 points as the pre-specified MCID for both.[19] Patient-reported treatment success was evaluated by VNS score (1–5, with ≥4 indicating success), patient-estimated repigmentation (<25%, 25–49%, 50–74%, >75%), and a binary global treatment assessment, mirroring the original VNS validation study.[20]

Statistical analysis

Categorical variables are reported as frequencies and percentages; continuous variables as mean ± SD or median [IQR] according to normality (Kolmogorov–Smirnov test). Associations between categorical variables and F-VASI75/90 were evaluated by chi-squared or Fisher's exact test; continuous variables between response groups were compared by Student's t-test or Mann–Whitney U test. Paired comparisons between 24 and 52 weeks were restricted to the 229 patients with assessments at both timepoints to account for differences in baseline disease severity, using McNemar and Wilcoxon tests. A sub-analysis was performed on season of initiation (March–May, "summer-group"; October–December, "winter-group"); those starting in other months were not included in this comparison. Multivariable logistic regression tested whether the seasonal association with F-VASI75 at 24 weeks was independent of baseline disease activity. Odds ratio (OR) and 95% confidence interval (CI) were estimated (details in Table S4). Missing data were assessed using Little's MCAR test, which confirmed a missing-completely-at-random mechanism; analyses involving variables with 20–30% missing values were pre-specified as available-case sub-analyses. No formal sample size calculation was performed; the

study enrolled all consecutive eligible patients treated at participating centres during the defined enrolment period. A two-sided p<0·05 was considered statistically significant. Analyses were performed in R version 4.3.3.

Results

Patient characteristics

Baseline characteristics are presented in Table 1. The cohort comprised 860 patients (mean age 47·4 ± 15·5 years; 58·1% female; mean disease duration 162·4 ± 152·0 months). Fitzpatrick phototype III was the most frequent (54·5%), and 84·3% had received prior vitiligo therapy. Autoimmune thyroiditis was the most common comorbidity (228, 26·5%). Disease activity data were available for 607 patients (70·6%), of whom 284 (46·8%) had active disease

Repigmentation outcomes

At 24 weeks, F-VASI75 was achieved by 159 patients (18·5%) and F-VASI90 by 49 (5·7%). F-VASI75 was unchanged when the analysis was restricted to patients receiving ruxolitinib monotherapy (18·5%; n=828), confirming that the small subgroup receiving concomitant phototherapy (32/860, 3·7%) did not materially affect the overall estimates (Table S5). Among the 229 patients with assessments at 24 and 52 weeks, F-VASI75 increased from 29·7% to 38·4% (McNemar p=0·003) and F-VASI90 from 4·4% to 25·8% (p<0·001); median ΔF-VASI deepened from 50·0% to 58·5% (p<0·001) (Figure 1). Total-body response followed

a parallel trajectory: T-VASI50 increased from 10·9% to 21·0% (p<0·001), though median ΔT-VASI did not differ significantly between timepoints (p=0·25) (Table 2).

In univariate analysis (Table 3), F-VASI75 responders at 24 weeks had significantly higher baseline disease activity (VSAS 5·5 vs 1·0; p<0·001), were older at disease onset (median 36 vs 30 years; p=0·026), and had a higher prevalence of non-autoimmune comorbidities (44·3% vs 33·0%; p=0·009). Baseline F-VASI and T-VASI did not differ between groups. Responders had markedly higher baseline DLQI (13·0 vs 7·0), GAD-7 (11·0 vs 6·0), and VitiQoL (59·0 vs 28·0; all p<0·001), consistent with greater overall disease burden; PHQ-9 did not differ (p=0·976). For F-VASI90 responders, additional associations included male sex (59·2% vs 40·8%; p=0·017) and shorter disease duration (median 72 vs 120 months; p=0·022). Sex, Fitzpatrick phototype, ethnicity, and baseline F-VASI were not associated with F-VASI75 (all p>0·05).

Stratification by baseline disease activity

Active-disease patients (n=284) had greater baseline T-VASI (7·00 vs 4·02; p<0·001) and DLQI (10·0 vs 6·0; p<0·001) compared with stable-disease patients (n=323), despite lower F-VASI (0·52 vs 0·80; p<0·001). Active disease was associated with superior repigmentation: F-VASI75 at 24 weeks was 22·5% vs 13·3% (p=0·004), and median ΔF-VASI at 24 weeks was 48·92% vs 38·68% (p<0·001). At 52 weeks, F-VASI75 rates converged (40·4% vs 31·5%; p=0·262), whereas F-VASI90 remained higher in the active group (33·3% vs 18·0%; p=0·026). Active disease was also associated with greater quality of life (QoL)

and mental health improvement at 52 weeks (ΔVitiQoL 100·0% vs 40·0%; ΔPHQ-9 100·0% vs 50·0%; both p<0·001).

Seasonal associations

Patients initiating ruxolitinib between March and May (summer group, n=52) were compared with those initiating between October and December (winter group, n=217); both groups included only patients on ruxolitinib monotherapy. They had comparable baseline disease extent (T-VASI 3·35 vs 4·00, p=0·092; F-VASI 0·65 vs 0·78, p=0·730) but significantly higher disease activity in the summer group (VSAS 3·00 vs 0·00; p<0·001) and greater baseline psychiatric burden (GAD-7 11·0 vs 5·0; VitiQoL 46·0 vs 27·5; both p<0·001). At 24 weeks, summer initiators achieved higher F-VASI75 (42·3% vs 13·4%; unadjusted OR 3·2, 95% CI 1·7–6·0; p<0·001) and greater improvements in anxiety and QoL (ΔGAD-7 73·0% vs 33·3%; ΔVitiQoL 69·2% vs 27·1%; both p<0·001); full VASI and PRO data are in Table S2. At 52 weeks, outcomes were comparable between groups (all p>0·09), though the small summer cohort (n=11) limits interpretation.

In multivariable logistic regression, summer-group (adjusted OR 6·7, 95% CI 2·7–16·8; p<0·001) and Koebner phenomenon (k-VSAS) at baseline (adjusted OR 1·6, 95% CI 1·04–2·66; p=0·042) were the only independent predictors of response. Full model estimates are provided in Supplementary Table S4. Overall, these seasonal findings should be regarded as exploratory and hypothesis-generating.

Patient-reported outcomes and quality of life

Patient-perceived benefit

VNS ≥4 was achieved in 197 (36·4%) patients at 24 weeks and 104 (55·9%) at 52 weeks. Concordance between patient-estimated and clinician-measured repigmentation is shown in Figures 2 and 3. At 24 weeks, 72·9% of patients with ΔF-VASI ≥75% correctly estimated ≥75% repigmentation, while 66·7% of those with ΔF-VASI <25% correctly estimated minimal improvement. At 52 weeks, concordance was maintained at high responses (59·7% with ΔF-VASI ≥75% estimating ≥75%) but was reduced in intermediate ΔF-VASI categories. Global treatment success was reported by 82·8% (367/443) at 24 weeks, and 96·4% (107/111) at 52 weeks.

Quality of life

DLQI improved from a median of 7·0 at baseline to 3·0 at 24 weeks and 2·0 at 52 weeks (both $p<0·001$), and VitiQoL from 32·0 to 11·0 and 1·5 (both $p<0·001$); the larger 52-week gain partly reflects the higher baseline burden of completers (T-VASI 10·2 vs 4·0; $p<0·001$). Full PRO data are reported in Table S1.

DLQI improvement correlated more strongly with total-body than facial repigmentation at both timepoints; VitiQoL showed stronger correlation with facial repigmentation at 24 weeks, with associations deepening through 52 weeks for both instruments (Table S3).

Mental health outcomes

At baseline, 37% of patients had moderate-to-severe anxiety (GAD-7 ≥10) and 19% had moderate-to-severe depressive symptoms (PHQ-9 ≥10). GAD-7, PHQ-9, and VitiQoL were strongly intercorrelated (rho 0·49–0·72). T-VASI showed a moderate association with DLQI (rho +0·38) and weak or non-significant associations with anxiety and depression. (Table S3) GAD-7 declined from a median of 6·0 at baseline to 3·0 at 24 weeks (Δ 43·7%; MCID 37·3%; p<0·001) and 3·0 at 52 weeks (Δ 63·1%; MCID 61·4%; p<0·001), indicating continued improvement in relative terms despite stable median value. PHQ-9 declined from 5·0 to 2·0 at 24 weeks (Δ 50·0%; MCID 33·2%; p<0·001) and 0·0 at 52 weeks (Δ 100·0%; MCID 51·6%; p<0·001). The proportion with moderate-to-severe anxiety fell to 11% at 24 weeks and 2% at 52 weeks; no patient remained in the severe GAD-7 category at 52 weeks. PHQ-9 followed a parallel trajectory from 19% at baseline to 7% and 1%. (Table S1) Mental health improvements were more closely associated with total-body than facial repigmentation at 24 weeks, with associations strengthening through 52 weeks. (Table S3)

Safety

Among 747 patients with documented adverse event status, 87 (11·6%) reported events. The most common were application-site acne and folliculitis (53, 60·9%) and pruritus (24, 27·5%); 86 of 87 graded events (98·9%) were mild. The median time to adverse event occurrence was 12·9 weeks (IQR 8·8–19·3 weeks), with 46·4% emerging before week 12 (with peak at 8–12 weeks) and 82·1% within 24 weeks. Acne appeared earliest (median 8.9 weeks, IQR 4·8–15·3).

Of 13 treatment discontinuations (1·5%), seven were temporary suspensions for adverse events, five were due to lack of effectiveness, and one was at patient preference (Table 4).

Discussion

This cohort of 860 patients treated with topical ruxolitinib in routine practice was more heterogeneous than registration-trial population, with greater comorbidity burden and 84% with prior treatment. Repigmentation improved progressively through 52 weeks and anxiety, depression, and disease-specific QoL improved in parallel. F-VASI75 at 24 weeks (18·5%) was lower than in TRuE-V studies (30·9%),[10,21] a difference more plausibly reflecting real-world constraints than reduced therapeutic potential. Including patients with baseline F-VASI below 0·5 (excluded from TRuE-V) did not account for this difference and the absence of phototype effects, in contrast to Seneschal et al.,[21] likely reflects limited variance in our cohort (54·5% Fitzpatrick type III) rather than a true biological null.

The most clinically meaningful finding is the treatment trajectory: repigmentation continued to deepen through 52 weeks, with paired analysis confirming a significant increase in F-VASI75 (29·7% to 38·4%) and F-VASI90 (4·4% to 25·8%) within the same patients without evidence of plateau or response loss. In TRuE-V1/2[10], F-VASI75 rose from 30·9% to 50·3% and F-VASI90 from 15·3% to 30·0% over the same interval, an absolute gain of similar magnitude achieved from a considerably higher starting point. Our cohort started from a lower baseline and near-universal prior treatment, yet generated absolute increments of comparable magnitude, consistent with the TRuE-V long-term extension

data[22] and suggesting this accumulation continues beyond the present observation window. VNS ≥4 rose from 36·4% at 24 weeks to 55·9% at 52 weeks, nearly double the TRuE-V rates (20·5–24·5%),[10] confirming that the clinical trajectory translates into benefit as experienced by patients. Baseline disease activity was associated with superior 24-week repigmentation despite greater overall disease burden. This finding is informative when contextualised against TRuE-V subgroup data, in which F-VASI75 at 52 weeks was only marginally higher in progressive than stable disease (52·7% vs 49·4%),[21] a non-significant difference. The more pronounced real-world differential likely reflects greater phenotypic heterogeneity in routine practice, where patients with long-standing stable disease — in whom perilesional melanocyte reservoir exhaustion,[23] chronic IFN-γ-driven senescence,[24] and reduced MMP-9 expression[25] may collectively constrain repigmentation potential — are under-represented in controlled trials. Heightened JAK-STAT activation in progressive disease may preserve a mobilisation-competent perilesional melanocyte pool, favouring both disease stabilisation and early.[23-25] Although F-VASI75 rates converged by 52 weeks, active disease remained associated with higher F-VASI90, supporting early intervention in this biological stage. The independent association of Koebner phenomenon with treatment response in multivariable analysis is consistent with this interpretation: Koebner positivity may reflect heightened epidermal inflammatory susceptibility and active JAK-STAT engagement, and its retention as an independent predictor after adjustment, whereas total disease activity did not, points to a signal that is not simply a marker of overall activity.The inflammatory biology of active vitiligo may also render treatment response sensitive to ambient ultraviolet (UV) exposure. Summer treatment initiation was

associated with markedly superior repigmentation at 24 weeks. In a Mediterranean country such as Italy, a March-May treatment start places most of the first 24 weeks of therapy within the high-UV season, when sun exposure is largely unavoidable even without intentional sun-seeking, unlike an October–December start, whose early treatment months carry minimal ambient UV. By mobilising melanocyte precursors from the follicular reservoir,[26] UV may provide a cellular substrate that JAK inhibition alone cannot generate, consistent with superior outcomes reported with ruxolitinib combined with narrowband UVB.[27] To our knowledge, this is the first real-world study to identify a seasonal association with topical ruxolitinib response. In multivariable analysis adjusting for disease activity, summer initiation remained an independent predictor of F-VASI75, suggesting the seasonal effect is not entirely explained by the higher baseline disease activity of summer-initiating patients. At 52 weeks, the advantage was no longer evident, consistent with reciprocal seasonal UV exposure inherent to the study design, though the small summer subgroup limits firm conclusions. Prospective studies with objective UV dosimetry are needed.

This study is the first real-world investigation to evaluate GAD-7, PHQ-9, and VitiQoL alongside clinical endpoints through 52 weeks of treatment. The baseline burden, while lower than the 55% moderate-to-severe PHQ-9 rate reported in the global VALIANT study,[3] was clinically substantial. The strong intercorrelations among GAD-7, PHQ-9, and VitiQoL at baseline suggest that anxiety, depression, and disease-specific quality of life represent interconnected rather than independent dimensions of psychosocial burden — a finding that reinforces the case for their joint assessment in routine vitiligo care. That cutaneous disease extent explained only a modest proportion of this burden, with T-VASI showing a

moderate association with DLQI but weak or non-significant associations with anxiety and depression, is consistent with evidence that lesion location, disease duration, and patient-level factors contribute to psychosocial impairment in vitiligo.[2,3]

During treatment, improvements in anxiety, depression, and quality of life tracked clinical repigmentation within individual patients, with associations between total-body repigmentation and mental health strengthening progressively through 52 weeks. This within-patient pattern is not at odds with the modest cross-sectional associations at baseline — the two reflect different phenomena: one the variance across a heterogeneous population, the other the individual trajectory of psychological measures alongside skin improvement. Direct comparison with TRuE-V1/2 is not possible, as GAD-7 and PHQ-9 were not evaluated in the phase 3 trials; notably, DLQI did not change significantly versus vehicle at 24 weeks in TRuE-V,[10] whereas in our cohort QoL improved progressively through 52 weeks. Two real-world studies have previously reported limited or early DLQI changes under topical ruxolitinib,[11,12] in contrast to the sustained trajectory observed here, most plausibly reflecting higher baseline burden in routine care where greater severity leaves more room for measurable gain.[28,29] DLQI remained stable from 52 weeks to 2 years in the TRuE-V extension,[22] supporting the durability of these gains. These improvements should be interpreted cautiously. In an uncontrolled cohort they cannot be attributed to ruxolitinib or to repigmentation alone, as closer dermatological follow-up, patients' expectations, regression to the mean, seasonal effects, and unmeasured psychological support may all have contributed. Taken together, these findings argue for standardised mental health

assessment as a routine component of vitiligo care and for psychiatric endpoints as co-primary outcomes in future trials.

The adverse event profile was confined to application-site reactions, of which 98·9% were mild, with a low treatment discontinuation rate (1·5%). The absence of systemic events observed in TRuE-V[10,30] most likely reflects lower ascertainment in routine practice rather than a genuine difference in event burden. Acneiform reactions emerged earliest, within the first 24 weeks, identifying this as the window of greatest clinical vigilance; temporary suspension alone or topical antibiotics was sufficient to allow continuation in most cases.

The main strengths are the sample size, national multicentre representation across 34 centres, and 52-week follow-up. We also assessed a broad set of clinical and patient-reported measures, as repigmentation, disease activity, quality of life and psychological distress, matching the core domains agreed for vitiligo by international consensus and used as the assessment standard for coordinated registries.[31,32] These domains reflect a psychosocial burden that is central to routine care but under-represented in registration trials. To our knowledge, the systematic longitudinal assessment of GAD-7, PHQ-9 and VitiQoL has not been reported before in a real-world ruxolitinib cohort.The retrospective design is the principal limitation. PRO data availability of 65–77% is expected in a real-world setting; Little's MCAR test confirmed missing data were missing completely at random, and PRO analyses were pre-specified as available-case sub-analyses. Information on concurrent mental-health treatment (psychotropic medication, counselling, or psychotherapy) was not systematically collected, and its potential contribution to the observed improvements in patient-reported outcomes cannot be

excluded. Adherence and the quantity of medication used were not systematically recorded, reflecting the retrospective, real-world design. The 52-week cohort reflects time of data lock, not response selection, and no patient reaching 52 weeks was excluded; nonetheless, patients with 52-week data had more active and extensive disease at baseline than those with 24-week follow-up only, which should be considered when interpreting the longer-term estimates. Residual confounding cannot be excluded: although summer initiation remained an independent predictor after adjustment for disease activity, the seasonal analysis cannot fully disentangle UV exposure from other characteristics of summer-initiating patients, particularly as individual data on sun exposure, sunscreen use, occupational outdoor activity, and geographic latitude were not available; prospective studies with objective UV dosimetry are needed. The Mediterranean context may limit generalisability to different geographic and healthcare settings.

Conclusion

In a large real-world cohort considerably more heterogeneous than those enrolled in registration trials, topical ruxolitinib was associated with progressive and sustained repigmentation through 52 weeks, with excellent tolerability. Active disease and summer initiation were associated with superior early response; given the observational design, these associations are exploratory and require prospective confirmation. Improvement in anxiety, depression, and disease-specific QoL accompanied repigmentation and, while they cannot be attributed to treatment in an uncontrolled cohort, support the routine

assessment of mental health in vitiligo care and warrant consideration of psychological endpoints in future trials.Prospective studies with objective UV dosimetry are needed to quantify the independent contribution of seasonal exposure.

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Figure legends

Figure 1. Representative facial repigmentation under Wood's lamp illumination in two patients with non-segmental vitiligo treated with topical ruxolitinib. Upper panels (a–c): patient 1 at baseline (a), week 24 (b), and week 52 (c), demonstrating gradual but sustained repigmentation of extensive facial involvement through 52 weeks. Lower panels (d–f): patient 2 at baseline (d), week 24 (e), and week 52 (f), showing progressive frontal, periorbital, and malar repigmentation Written informed consent for publication of clinical photographs was obtained from both patients.

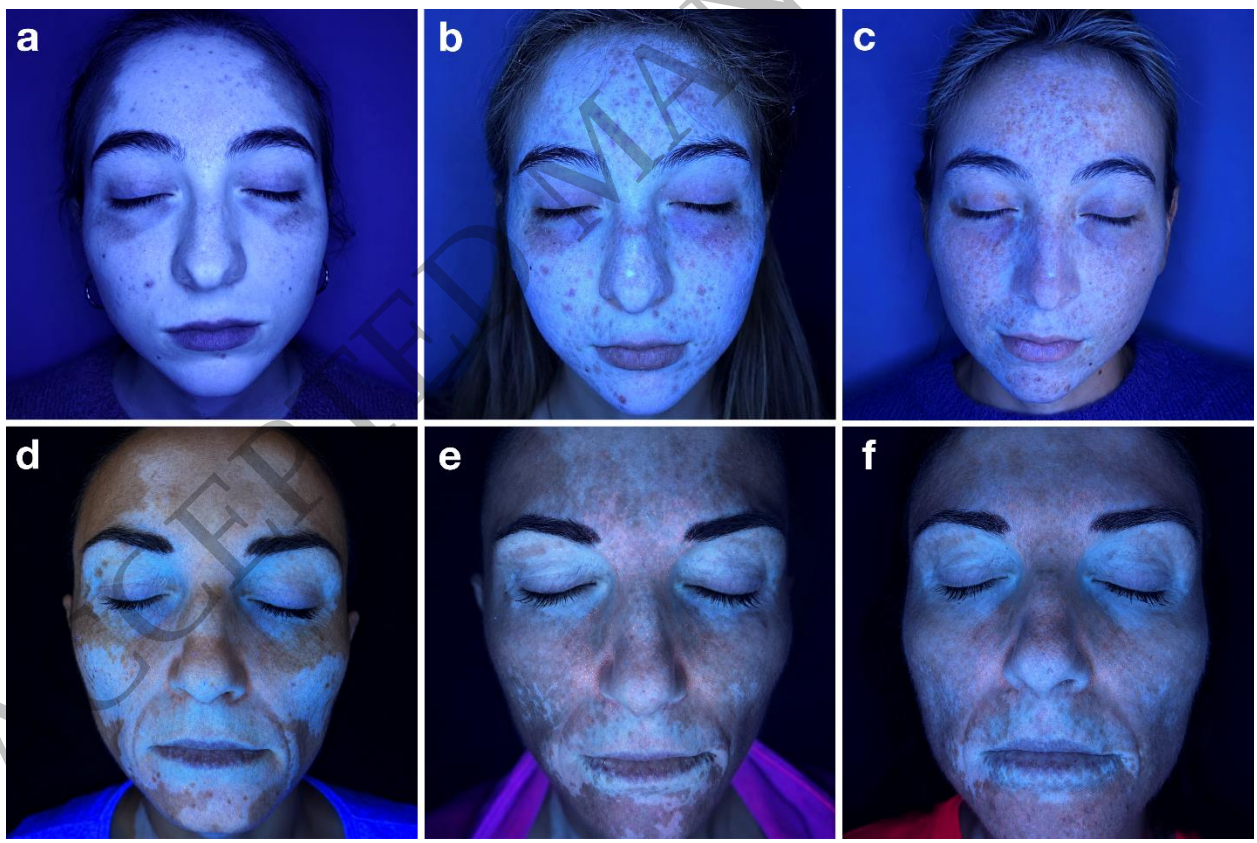


Figure 2. Concordance between patient-reported and physician-assessed (F-VASI) repigmentation responses at 24 weeks. Each cell shows the percentage of patients within each patient-reported repigmentation category who achieved the corresponding F-VASI range. The diagonal distribution reflects the degree of agreement between objective and subjective assessments.

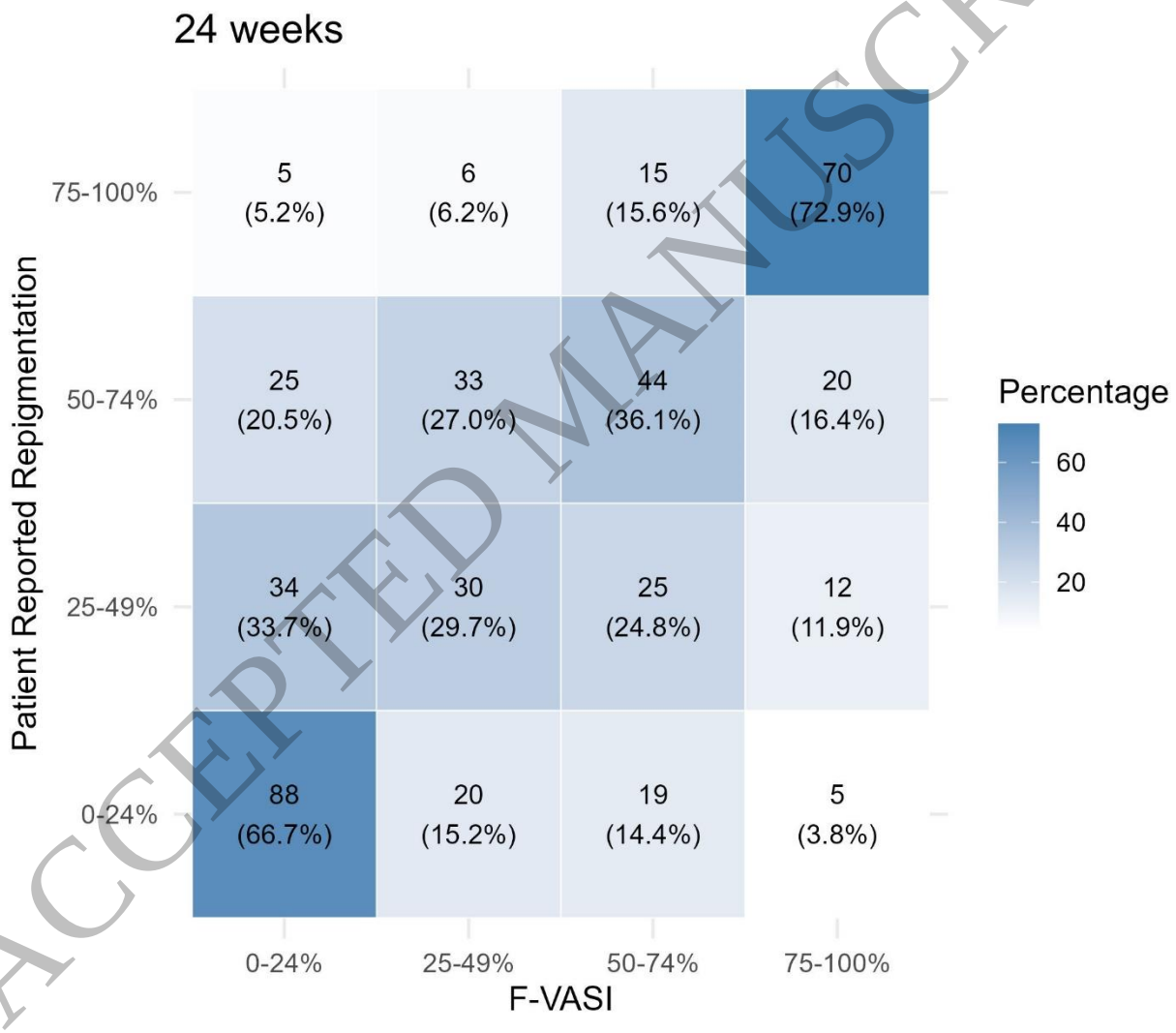
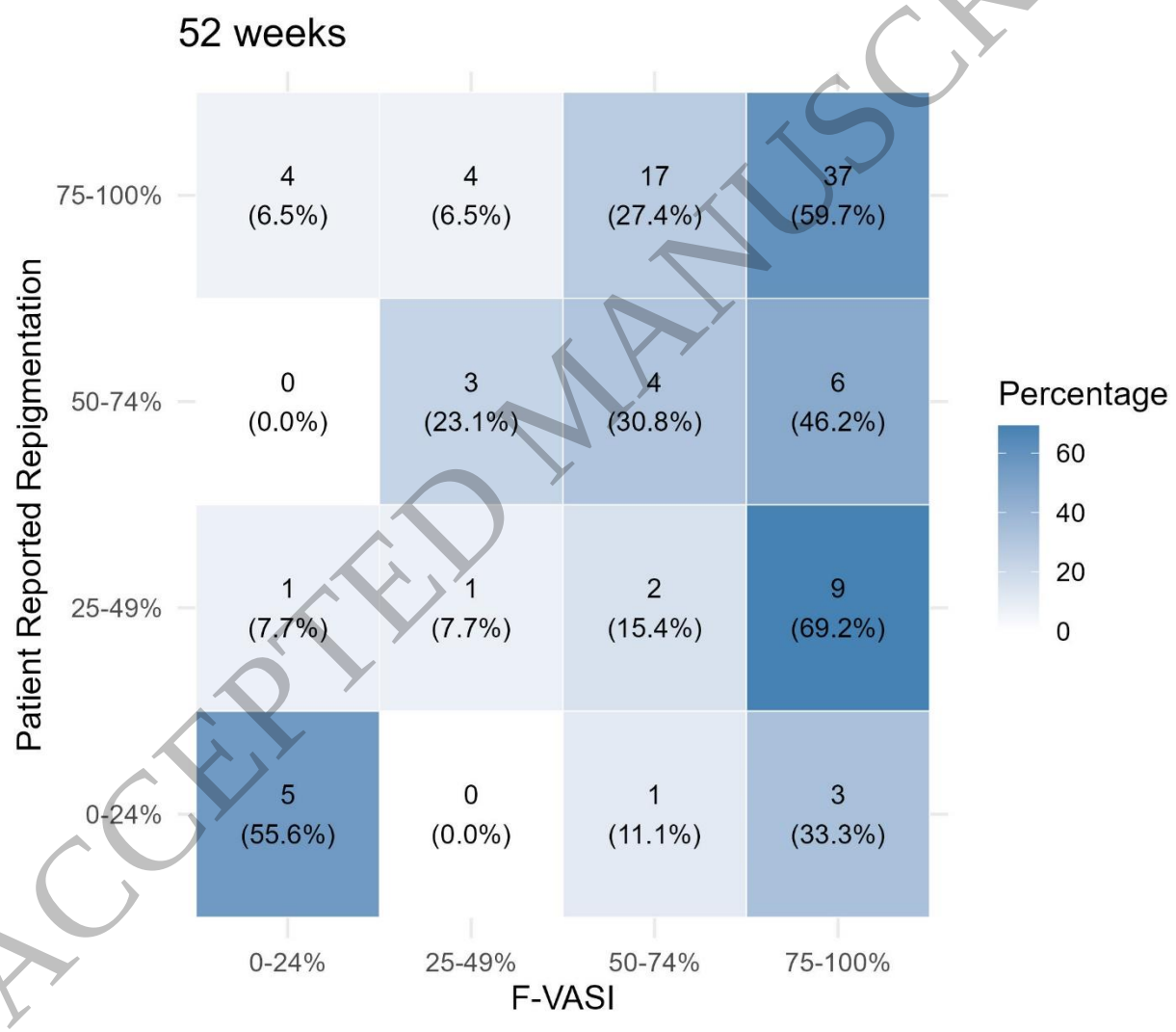


Figure 3. Concordance between patient-reported and physician-assessed (F-VASI) repigmentation responses at 52 weeks. Each cell shows the percentage of patients within each patient-reported repigmentation category who achieved the corresponding F-VASI range. The diagonal distribution reflects the degree of agreement between objective and subjective assessments.



1 **Table 1. Baseline characteristics of the study cohort**

Characteristic	n = 860
Demographics	
Age at baseline (years), mean ± SD	47·4 ± 15·5
≤17 years, n (%)	41 (4·8)
18–64 years, n (%)	713 (82·9)
≥65 years, n (%)	106 (12·3)
Female sex, n (%)	500 (58·1)
Fitzpatrick phototype (n=752), n (%)	
I–II (fair skin)	259 (34·4)
III (intermediate)	410 (54·5)
IV–VI (dark skin)	83 (11·0)
Disease characteristics	
Age at disease onset (years), mean ± SD	32·4 ± 16·0
Disease duration (months), mean ± SD	162·4 ± 152·0
Active disease (n=607 with data), n (%)	284 (46·8)
F-VASI, median [IQR]	0·70 [0·30–1·50]
T-VASI, median [IQR]	4·68 [2·10–9·60]
VSAS total score, median [IQR]	2·0 [0·0–6·0]
Leucotrichia, n (%)	117 (13·6)
Sutton naevi, n (%)	96 (11·2)
Baseline patient-reported outcomes*, median [IQR]	
DLQI (n=666)	7·0 [3·0–15·0]

GAD-7 (n=584)	6·0 [3·0–12·0]
PHQ-9 (n=557)	5·0 [2·0–8·0]
VitiQoL (n=616)	32·0 [14·0–54·0]
Medical history	
Any associated autoimmune disease, n (%)	311 (36·2)
Autoimmune thyroiditis	228 (26·5)
Other autoimmune conditions†	83 (9·7)
Non-autoimmune comorbidities, n (%)	300 (35·0)
Concomitant medications (n=806), n (%)	350 (43·4)
Previous vitiligo treatments	
Any prior treatment, n (%)	724 (84·3)
Narrowband UVB phototherapy	447 (52·6)
Topical tacrolimus	280 (32·9)
Other topical corticosteroids	250 (29·4)
Topical clobetasol	187 (22·0)
Systemic corticosteroids	63 (7·4)
Treatment at baseline	
Ruxolitinib monotherapy, n (%)	828 (96·3)
Ruxolitinib + narrowband UVB, n (%)	32 (3·7)

SD, standard deviation; IQR, interquartile range; F-VASI, Facial Vitiligo Area Scoring Index; T-VASI, Total-body Vitiligo Area Scoring Index; VSAS, Vitiligo Signs of Activity Score; DLQI, Dermatology Life Quality Index; GAD-7, Generalized Anxiety Disorder 7-item scale; PHQ-9, Patient Health Questionnaire-9; VitiQoL, vitiligo-specific quality-of-life scale.

* Baseline PRO data were available for 666/860 (77%) patients for DLQI, 584/860 (68%) for GAD-7, 557/860 (65%) for PHQ-9, and 616/860 (72%) for VitiQoL.

† Includes: Type 1 diabetes (n=15), Graves' disease (n=10), rheumatoid arthritis (n=13), coeliac disease (n=11), alopecia areata (n=8), autoimmune atrophic gastritis (n=7), connective tissue disease/SLE/Sjögren (n=13), inflammatory bowel disease (n=3), myasthenia gravis (n=1), autoimmune urticaria (n=1), lichen sclerosus atrophicus (n=1)

Table 2. Effectiveness outcomes at 24 and 52 weeks

Outcome	24 weeks (n=860)	24 weeks paired (n=229)	52 weeks (n=229)
Facial VASI — primary endpoints			
F-VASI75 (≥75% improvement), n (%)	159 (18·5%)	68 (29·7%)	88 (38·4%)
F-VASI90 (≥90% improvement), n (%)	49 (5·7%)	10 (4·4%)	59 (25·8%)
ΔF-VASI (%), median [IQR]	48·0 [20·0–66·7]	50·0 [42·1–78·7]	58·5 [50·0–90·0]
Total-body VASI			
T-VASI50 (≥50% improvement), n (%)	126/760 (16·6%)	25 (10·9%)	48 (21·0%)
ΔT-VASI (%), median [IQR]	21·0 [0·0–44·9]	32·7 [4·4–48·8]	25·6 [14·6–54·8]

F-VASI75/90: ≥75% or ≥90% improvement from baseline in Facial VASI. T-VASI50: ≥50% improvement from baseline in total VASI. The paired cohort (n=229) comprises patients with assessments at both 24 and 52 weeks; their 24-week values are reported separately from the primary analysis owing to differences in baseline disease severity. CI, confidence interval; IQR, interquartile range.

Table 3. Baseline characteristics associated with F-VASI75 response at 24 weeks: univariate analysis

Characteristic	Non-responders (n=701)	Responders (n=159)	p value
Clinical characteristics			
Age at onset (years), median [IQR]	30·0 [18–43]	36·0 [21–45·5]	0·026
Sex (male), n (%)	290 (41·4)	70 (44·0)	0·600
Fitzpatrick phototype (III-VI), n (%)	484 (69·0)	117 (73·6)	0·303
Disease duration (months), median [IQR]	108 [48·00–240·00]	132 [48·00–228·00]	0·487
VSAS total score, median [IQR]	1·0 [0·0–5·0]	5·5 [1·0–14·0]	<0·001
c-VSAS score, median [IQR]	0·0 [0·0–2·0]	4·0 [0·0–11·0]	<0·001
k-VSAS score, median [IQR]	0·0 [0·0–1·0]	4·0 [0·0–14·0]	<0·001
h-VSAS score, median [IQR]	0·0 [0·0–2·0]	3·0 [0·0–14·0]	<0·001
New lesions (6 months), n (%)	172/560 (30·7)	57/112 (50·9)	<0·001
F-VASI, median [IQR]	0·73 [0·36–1·50]	0·59 [0·24–1·50]	0·252
T-VASI, median [IQR]	4·66 [2·34–9·00]	5·50 [1·55–11·35]	0·841
Autoimmune comorbidities, n (%)	194 (27·8)	54 (34·2)	0·134
Non-autoimmune comorbidities, n (%)	230 (33·0)	70 (44·3)	0·009
Baseline patient-reported outcomes, median [IQR]			
DLQI	7·0 [2·0–12·0]	13·0 [3·8–25·0]	<0·001
GAD-7	6·0 [3·0–11·0]	11·0 [5·0–15·0]	<0·001
PHQ-9	4·0 [2·0–8·0]	5·0 [2·0–7·0]	0·976
VitiQoL	28·0 [12·0–49·5]	59·0 [30·0–71·0]	<0·001

Percentages for categorical variables are calculated on non-missing observations; denominators are shown where data were incomplete. c-VSAS, confetti depigmentation subscore; k-VSAS, Koebner phenomenon subscore; h-VSAS, hypochromia subscore of the Vitiligo Signs of Activity Score.

Table 4. Safety and tolerability profile (n=860)

Safety parameter	n=860	Timing (median, weeks)
Overall assessment		
Patients with documented AE status	747 (86·9%)	
No adverse events	660/747 (88·3%)	
Any adverse event	87/747 (11·6%)	
Specific adverse event types (n=87)		
Application-site acne and folliculitis	53 (60·9%)	8·9 (IQR 4·8–15·3)
Application-site pruritus	24 (27·5%)	14·2 (IQR 11·0–19·2)
Application-site exfoliation	3 (3·4%)	25·9 (IQR 25·9–26·0)
Application-site erythema	5 (5·7%)	12·0 (IQR 12·0–13·1)
Application-site burning	2 (2·3%)	13·0 (IQR 12·0–14·0)
Severity grading (n=87)		
Mild	86 (98·9%)	
Moderate	1 (1·1%)	
Severe	0 (0·0%)	
Adverse event management (n=59)		
No treatment required	20 (33·8%)	
Temporary drug suspension	7 (11·9%)	
Emollients	9 (15·2%)	

Topical antibiotic therapy	18 (30·5%)	
Systemic antibiotics	4 (6·8%)	
Topical adapalene	1 (1·7%)	
Treatment discontinuation (n=860)		
Any discontinuation	13 (1·5%)	
Temporary suspension for AE	7/13 (53·8%)	
Lack of effectiveness (not AE-related)	5/13 (38·5%)	
Patient preference	1/13 (7·7%)	

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